ADVANCES IN REPTILE CLINICAL THERAPEUTICS

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Abstract

The standard of today's reptile practice calls on clinicians to use an ever-increasing array of diagnostic tools to gather information and obtain a definitive diagnosis. Few, if any, pathognomonic signs exist for reptile diseases, and for most clinical syndromes there is a lack of information regarding pathophysiology for one to define standard therapeutic protocols based solely on clinical signs without objective diagnostic information. For example, in the relatively distant past, clinicians treating reptile patients would routinely administer parenteral calcium to green iguanas (*Iguana iguana*) with the primary presenting clinical sign of muscle tremors. Today, veterinarians who treat reptiles recognize that the risk of soft tissue mineralization and permanent damage to arteries, renal tubules, and other tissues usually outweighs the potential short-term benefit of calcium therapy. Before calcium therapy is initiated, it is best to know the patient's ionized calcium concentration to reduce the risk of potential adverse therapeutic side effects. A problem-oriented diagnostic approach directed toward minimizing risk and maximizing therapeutic benefit is now the standard of reptile practice.

Key words: antibiotic; antifungal; antiparasitic; antiviral; reptiles; therapy; treatment

Similar to the class Mammalia, the class Reptilia includes a diverse group of species, each with a unique pharmacologic response to every chemotherapeutic agent. As a result, therapeutic safety and efficacy differ among species. Unlike mammals, conscious reptiles are ectothermic, so physiologic and biochemical processes are strongly influenced by body temperature.[1] Reasonable assumptions about each individual reptile species' metabolism and immune response can be determined only under certain conditions. In most cases, before therapeutic agents are administered, the body temperature of a reptile patient must match that of the subjects in a given pharmacokinetic study, if available. The proper body temperature helps increase the chance of duplicating the findings of the study, although pharmacokinetics and pharmacodynamics do not necessarily vary at different patient body temperatures.[2-5] The veterinarian should be knowledgeable of species-specific pharmacokinetics, pharmacodynamics, therapeutic efficacy, and environmental requirements before treating the animal. This is not only to predict absorption, distribution, metabolism, excretion, and the therapeutic window of the drug(s) but also to meet the environmental needs of a reptile to maximize healing and the animal's immune response.[4,6,7] Published doses are available for many drugs, and these may have been selected empirically, calculated with the use of allometric or other scaling technique, or obtained from published pharmacokinetic research data. It is incumbent on the clinician to evaluate whether a published dose would be safe and effective in a particular clinical case. Dosage, dosing interval, and route of administration must be evaluated on a case-by-case basis. Consult up-to-date, peer-reviewed literature to identify the species of reptile being treated and their environmental needs, optimal body temperature, and the pharmacokinetics and pharmacodynamics of the drug(s) to be used.[8]

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Managed thermoregulation, hydration, and nutrition are paramount for safe, effective drug therapy. Thermal options and gradients must be provided for conscious, active reptiles to thermoregulate with body temperature being monitored during the treatment period. In cases of weakness and decreased activity, thermoregulation of the patient should be actively managed as part of the therapeutic plan. Dehydrated, anorexic reptiles may not absorb, distribute, metabolize, or eliminate chemotherapeutic agents in the same manner as the healthy animals tested under controlled conditions in pharmacologic research. Thus, nursing care of dehydrated reptile patients also includes management of body fluids, electrolytes, and nutrition.

Most of the drugs used to treat reptiles are considered "extralabel" as relatively few therapeutic agents are approved for use in these species. In the United States, the Animal Medicinal Drug Use Clarification Act of 1994 and the Minor Use and Minor Species Animal Health Act of 2004 serve as guides for extralabel drug use. Prescription drugs may be used to treat disease in reptiles under the supervision of a veterinarian if (1) they are approved by the US Food and Drug Administration (FDA) for any purpose in any species, (2) a valid veterinarian-client-patient relationship exists, and (3) the FDA has not specifically prohibited extralabel use of the drug. Certain medical record and prescription label requirements must be followed to meet the regulatory obligations of veterinary licensure.[9]

ADMINISTRATION AND DOSING

Dosage and route of administration are determined by the chemical, pharmacokinetic, and pharmcodynamic properties of every drug for each species. Numerous studies have been performed to understand the mechanism of action, therapeutic window, absorption, distribution, metabolism, and excretion variables of some drugs in some reptile species. However, many questions remain unanswered about the scientific basis for drug use in reptile species commonly maintained in captivity, so informed, empirical dosing is still necessary in many cases.[8] Veterinarians administer therapeutic agents to reptiles via oral (PO), enteral, subcutaneous (SC), intramuscular (IM), intravenous (IV), intracoelomic, intratracheal, intrapulmonary, intraosseous, intraperitoneal, intrathecal, and intracardiac routes, as well as via nebulization. Parenteral administration is considered more reliable than the enteral route for therapeutic efficacy in reptile patients.[4] Sufficient evidence exists to support administration of most parenteral drugs in the cranial half of the body, when possible, to avoid the first-pass effect of drugs that are eliminated via renal tubular excretion or hepatic metabolism. Venous blood from the caudal half of the body enters the caudal vena cava through either the renal portal system and peritubular capillaries or the hepatic portal system from the abdominal or mesenteric veins and hepatocellular parenchyma.[10,11] Giving therapeutic agents in the caudal half of the body is acceptable for a few specific products and may be considered for other drugs when the cranial half is not available.[5,12,13] When giving drugs in the caudal half of a reptile patient's body, dosage is adjusted to account for the renal or hepatic first-pass effect. Intracoelomic administration of fluids or systemic drugs is not recommended. Absorption across coelomic membranes is difficult to assess in clinical patients and is not guaranteed, particularly in cases of abnormal blood proteins, coelomitis, or ascites. Intracoelomic administration of therapeutic agents has resulted in accidental needle puncture or laceration of an internal organ and accidental deposition of the agent into the intestines, reproductive tract, or urinary bladder.[14] Some therapeutic challenges in reptiles can be overcome by novel approaches to drug administration, including osmotic pump, dermal patch, depot formulation, vascular access port, and topical administration.

Osmotic Pump

Alzet osmotic pumps (DURECT Corp, Cupertino, CA USA) are implanted, miniature infusion pumps designed for continuous infusion of therapeutic agents to unrestrained animals. They are available with fixed delivery rates between 0.11 and 10 μL/h, with delivery durations between 1 day and 6 weeks. Marketed for laboratory animals, osmotic pumps range in size from 15 to 51 mm in length and 6 to 14 mm in diameter and have been used to deliver dozens of different therapeutic agents.[15] The "pumps" operate via an osmotic pressure difference between the tissue environment and a salt-containing osmotic sleeve. The high osmolality of the salt sleeve causes water to diffuse into the pump, across the outer semipermeable membrane and into the salt sleeve, which applies pressure on a flexible (impermeable) internal reservoir that contains the therapeutic agent. This pressure causes